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10/803,132	03/17/2004	Matthew M. Tanzer	2160US	6137

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EXAMINER	
BULL, CHRISTOPHER	

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/803,132	TANZER ET AL.	
	Examiner	Art Unit	
	Christopher Bull	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *6-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, Claims 1-5, in the reply filed on October 31, 2005 is acknowledged.

Abbreviations used include:

PBG deaminase = Porphobilinogen Deaminase

PBGD = the gene encoding a PBG deaminase.

Claim Rejections - 35 USC § 112 First

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under the first paragraph of 35 U.S.C. 112 as lacking adequate written description.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention.*

In the instant case, the claims are drawn to methods of screening test compounds for their ability to bind to PBG deaminase polypeptides. The specification (page 10) defines these polypeptides as:

"a chain of at least two amino acids joined by peptide bonds. The chain may be linear, circular or combinations thereof. The polypeptides may contain amino acid analogs and other modifications, including, but not limited to glycosylated or phosphorylated residues."

The specification further states about PBG deaminase fragments on page 14, line 125:

"The fragments compose at least 10 consecutive amino acids of a PBG deaminase."

The specification further states about PBG deaminase activity on page 12, line 27:

"In addition, it is preferred that polypeptides of the invention have at least 10% of the activity of *M. grisea* PBG deaminase (SEQ ID NO:3) protein."

Applying all definitions, these claims read on any and all polypeptide fragments having at least ten consecutive amino acids of any PBG deaminase (Claim 1), of any fungal PBG deaminase

(Claim 2), or a *Magnaporthe grisea* PBG deaminase (Claims 3-5), and any unspecified variants or modifications thereof, that catalyze the reaction of PBG deaminase.

Considering the written description requirements:

(1) Level of skill and knowledge in the art:

The level of skill in the art at the time the invention was made was high in regards to making specific polypeptides, and conducting binding assays. However, skill at predicting of the effects of mutational substitution in a full-length polypeptide upon enzymatic activity was but modest, while that in predicting which shorter fragments will retain activity was poor. Further, the effects of modifications, insertions or deletions upon activity or binding were (and still are) unpredictable. The full-length sequences of PBG deaminase from *Saccharomyces cerevisiae* and other microbial, plant and mammalian sources were known (Disclosure page 8, line 19-20). A crystal structure from *E. coli* was known, as well as the structure of a covalently bound dipyrromethane cofactor that the enzyme itself synthesizes (Awan et al., 1997).

(2) Partial structure:

Applicants disclosed the full-length sequence of a *Magnaporthe grisea* PBG, but have not supplied any guidance as to what regions may be fragmented, nor what substitutions, modification, deletions or insertions may be made, with any reasonable expectation of successfully retaining activity or binding.

(3) Physical and/or chemical properties:

Applicants did not disclose isolating the *Magnaporthe grisea* PBG, nor report any physical or chemical properties of the enzyme. No examples have been provided of the preparation of any fragments, variants or modifications thereof.

(4) Functional characteristics:

No binding studies were reported on purified or unpurified full-length enzyme or any fragments, variants or modifications thereof. No examples of compounds being screened using the proposed methods were provided. Furthermore, no catalytic activity measurements on PBG deaminase from *Magnaporthe grisea* were given in the disclosure. Thus, it is unclear how the skilled artisan would know whether a given PBG deaminase polypeptide "had at least 10% of the activity of SEQ ID#3", as recited in Claim 5.

(5) Method of making the claimed invention:

No guidance in performing binding studies, or in preparation or isolation of the enzyme was given. No example or guidance is given for any other species of *Magnaporthe*, or for other genera of fungi, or any other organism.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claims 1-5 are broadly generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of polypeptides. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to

reflect this variance in the genus since the specification does not provide any examples of derivatives. While having written description of a *Magnaporthe grisea* PBG deaminase in the specification tables and/or examples, the specification is void of any other PBG deaminase sources, and of polypeptides, organic molecules that qualify for the functional characteristics claimed as the biomolecules, and polymers with functional characteristics that qualify.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claims 1-5 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for binding to a full-length *Magnaporthe grisea* PBG, does not reasonably provide enablement for using a PBG deaminase from other fungal species (Claims 2), or for a PBG deaminase from any source (Claim 1), or for any fragments, substitutions, modification, deletions or insertions thereof (references to "polypeptide" defined as broadly as in instant application in Claims 1-5). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make or use the invention commensurate in scope with these claims. The reasons are identical to those given above for Written Description.

Considering the state of the art as discussed by Applicants (Specification pages 2 & 3) and the high unpredictability and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to extend this method to other species and genera, and for any fragments, substitutions, modification, deletions or insertions to PBGs thereof.

Accordingly, it would take undue experimentation without a reasonable expectation of success to practice the claimed invention commensurate with the scope of the claims.

Claim Rejections - 35 USC § 112 Second

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the limitation " a polypeptide ... having at least 10% of the activity of SEQ ID#3;" in parts iii and iv. Since neither disclosure nor claims recite any quantitative measure of activity associated with SEQ ID#3, and since there is no reference to or incorporation of material measurement of the level of activity in a *Magnaporthe grisea* PBG, it is unclear as to what level of activity is being defined. Further, there is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated independently by Smythe et al. (1988) or Shioi et al. (1980) or Awan et al. (1997).

Claim 1 recites a method of identifying a test compound comprising the steps of: a) contacting a PBG deaminase polypeptide with a test compound and; b) detecting binding between the test compound and said PBG deaminase polypeptide. No steps are recited in Claim 1 wherein the test compound is required to demonstrate antifungal activity.

The methods of Smythe et al. or Shioi et al. or Awan et al. (1997) involved preparing an affinity chromatography column derivatized with compounds that selectively bind PBG deaminase protein (Cibacron Blue F3G, porphobilinogen and Mimetic Orange, resp.). For example, Smythe et al. achieved a 10-fold purification using this affinity column. Awan et al. purified the apo-enzyme (no dipyrromethane cofactor) in a single step using the Mimetic Orange affinity column, and showed that the presence of the cofactor dramatically lowered the affinity of the holoenzyme for the affinity column (page 9276 left column, lower third). Although Smythe et al. or Shioi et al. or Awan et al. (1997) were not intending to screen compounds for binding to PBG deaminase and thereby find candidates for antifungal activity, both steps of Claim 1 as instantly claimed read directly upon either reference.

Accordingly, each cited reference is deemed to anticipate the invention of Claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bacot et al. (6,074,830 June 13, 2000), in view of Levin et al. (US 6,294,345 Sept. 25, 2001).

Bacot et al. (Abstract, Col 6, lines 5-23) beneficially teach methods of screening compounds as fungicides using a *Magnaporthe grisea* polypeptide having the activity of 3,4-dihydroxy-2-butanone 4-phosphate synthase, which is a required enzyme in the riboflavin biosynthetic pathway. Bacot et al. do not teach this method using *Magnaporthe grisea* PBG deaminase polypeptides.

Levin et al. beneficially teach (Claim 1) a method of using PBG deaminase polypeptides from *Arabidopsis thaliana* to screen test herbicide compounds for PBG deaminase binding. Although this organism is a plant and not a fungus, Levin et al. beneficially provide motivation to produce a PBG deaminase polypeptide in any host cell (Col 2, line 55-56), and to use such PBG deaminase polypeptides in screening test compounds for binding to this known and essential enzyme as potential inhibitors (Col. 2, lines 57-63). They also beneficially indicate that the method is applicable to other essential enzymes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a *Magnaporthe grisea* polypeptide having the activity of PBG deaminase within the fungicide screening assay taught by Bacot et al., because each enzyme was known to be required for growth of the fungal organism. Further, one could expect success at screening potential compounds for binding to *Magnaporthe grisea* PBG deaminase polypeptides, based upon the beneficial teachings provided by the cited references, as discussed above. The adjustment of particular conventional working conditions (e.g., choosing a protein known to be essential for normal development, monitoring for binding as a method of screening for interactions, and/or determining a result-effective level of a potential inhibitor) is deemed merely

a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Bull whose telephone number is (571) 272-1327. The examiner can normally be reached on 7:30-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for Art Unit 1655 where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER